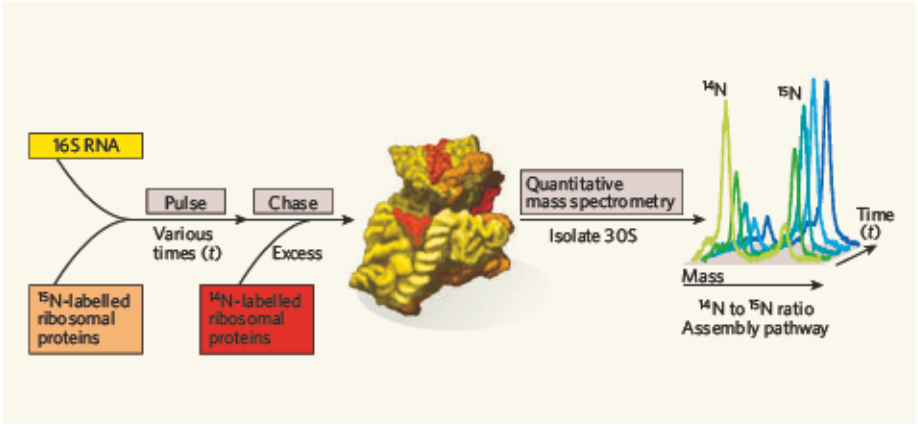

Figure 1 | Tracking assembly of the 30S ribosome in real time. 16S rRNA and twenty ^{15}N-labelled 30S proteins are mixed together *in vitro* to begin assembly of the ribosome. After a set period of time (t), further binding of ^{15}N-protein is inhibited by the addition of excess ^{14}N-labelled proteins. Once the assembly reaction is complete, the 30S complexes are isolated by centrifugation and analysed by mass spectrometry. The isotopic ratios of the ribosomal proteins at various times determine the order in which they join the complex, giving the 30S ribosome assembly map.

complexes. First, by purifying 30S particles before mass spectrometry, contributions from 'dead-end' intermediates are excluded. Second, simultaneous analysis of all 20 small-subunit proteins allowed the authors to use native proteins from cells grown in ^{15}N media, avoiding the need to overexpress individual proteins. The PC/QMS approach is attractively simple, and in principle can probably be adapted to examine many large RNA and protein complexes. The main requirements are reconstitution of the functional complex and the ability to label proteins using heavy isotopes or some other mass tag.

Given what we know about 30S ribosome assembly, what can be learnt from the protein association rates? Nomura and colleagues[9] observed that reconstitution at 30 °C stalls at an intermediate (RI) that lacks a subset of the 30S proteins. Thermal activation of RI at 42 °C has been correlated with refolding of the 16S rRNA near the centre of the 30S subunit[8]. If the rate of 30S assembly is limited by a single step, proteins that bind to the 16S rRNA after this rate-determining step should associate more slowly than those that bind before it and show a similar activation enthalpy.

By contrast, Talkington *et al.* find that neither the apparent association rate nor the activation enthalpy of binding correlate with the position of the protein in the assembly map. Instead, their results suggest that multiple rate-limiting steps control the kinetics of ribosome assembly. This is consistent with individual ribosomes taking alternative routes to the final structure.

Further work is needed to determine whether 30S assembly requires specific intermediates, or whether reconstitution intermediates represent meta-stable structures in a complex free-energy landscape. In simpler RNAs, meta-stable folding intermediates are observed when the RNA is kinetically trapped in misfolded structures[10,11]. However, some RNA molecules fold by alternative paths that avoid these trapped intermediates[10,12]. In the PC/QMS experiments, such stalled intermediates might have been missed because ^{15}N proteins that bind weakly to stalled intermediates could be washed out by the ^{14}N chase.

In the soft world of biological materials, cooperativity and specificity are achieved by the induced fit of molecular interfaces; that is, as two or more components come into contact they mould around one another to create stronger, more specific junctions. The idea that ribosome assembly can follow more than one path is consistent with redundant cooperative linkages in the assembly map[5]. These cooperative linkages ensure that individual complexes are assembled completely. They also create alternative kinetic paths that make the assembly process itself more robust. In the ribosome, these interactions have been fine-tuned through billions of years of evolution, providing a clear window into the world of cellular machines. ■

Sarah A. Woodson is in the T. C. Jenkins Department of Biophysics, Johns Hopkins University, 3400 North Charles Street, Baltimore, Maryland 21218, USA.
e-mail: swoodson@jhu.edu

1. Talkington, M. W. T., Siuzdak, G. & Williamson, J. R. *Nature* **438**, 628–632 (2005).
2. Ramakrishnan, V. & Moore, P. B. *Curr. Opin. Struct. Biol.* **11**, 144–154 (2001).
3. Nierhaus, K. H. *Biochimie* **73**, 739–755 (1991).
4. Warner, J. R. *Trends Biochem. Sci.* **24**, 437–440 (1999).
5. Nomura, M. *Science* **179**, 864–873 (1973).
6. Culver, G. M. *Biopolymers* **68**, 234–249 (2003).
7. Powers, T., Daubresse, G. & Noller, H. F. *J. Mol. Biol.* **232**, 362–374 (1993).
8. Holmes, K. L. & Culver, G. M. *Nature Struct. Mol. Biol.* **11**, 179–186 (2004).
9. Traub, P. & Nomura, M. *J. Mol. Biol.* **40**, 391–413 (1969).
10. Pan, J., Thirumalai, D. & Woodson, S. A. *J. Mol. Biol.* **273**, 7–13 (1997).
11. Treiber, D. K. & Williamson, J. R. *Curr. Opin. Struct. Biol.* **9**, 339–345 (1999).
12. Zhuang, X. *et al. Science* **288**, 2048–2051 (2000).

50 YEARS AGO

This is the centenary year of the Meteorological Office, and through its long record meteorologists have been confronted with dynamical problems of such complexity that their solution has sometimes seemed beyond hope. In recent years, however, nothing less than a revolution has taken place... The staff of the Napier Shaw Research Laboratory of the Meteorological Office...have shown that weather maps giving isobars and upper air contours may be predicted for 24 hr. ahead.

From *Nature* 3 December 1955.

100 YEARS AGO

Nature Through Microscope and Camera. By Richard Kerr. One of the many ways of beginning the study of natural science is with a "beauty-feast" — of flowers or birds, of shells or gems, of anything — for all natural things are beautiful, in their proper setting at least. It is an old-fashioned mode of approach, commending itself to children and simple minds, but one which often leads far beyond aesthetic pleasure to the joy of understanding. It affords a dynamic to investigation, and fosters a healthy reverence for things. Indeed, if we had to choose, we should prefer admiration without science to science without admiration. But a simple book like that before us shows that there is no necessary antithesis; it is a disclosure of beautiful things, and yet within its limits it is quite scientific.

The author's aim is to illustrate with well chosen examples the beauty of minute structure, the beauty which the microscope discloses, and he is to be congratulated on his success... we are here brought into close quarters with the familiar, with diatoms and Foraminifera, the whelk's radula and the barnacle's cirri, the butterfly's "tongue" and the scales of the sole... The photographs were taken by Mr. Arthur E. Smith, and are certainly among the finest that have ever been published.

From *Nature* 30 November 1905.

50 & 100 YEARS AGO